Paper No. 28

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ARTHUR A. BRANSTROM, DONATA R. SIZEMORE, and JERALD C. SADOFF

Appeal No. 2001-1881
Application No. 08/711,961

ON BRIEF

Before WINTERS, ADAMS, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 45 through 55. Claims 45 and 53 are representative of the subject matter on appeal, and read as follows:

45. A method for the delivery of exogenous DNA capable of being expressed in an animal cell, said method comprising:

(i) introducing said DNA into mutated bacteria, said bacteria having an attenuating factor which will result in lysis of the bacteria after entry into said cell; and

(ii) administering said bacteria to said cell, such that the bacteria, once inside the cell, will lyse, thereby delivering to the cell the DNA capable of being expressed therein.

53. A method for delivering DNA capable of being expressed in a mucosal epithelium cell, said method comprising:

(i) introducing said DNA into a mutated strain of Shigella which is unable to synthesize active aspartate β-semialdehyde dehydrogenase of the DAP pathway; and

(ii) administering the Shigella of (i) to a mucosal epithelium cell such that the Shigella, after uptake by said cell, will lyse, thereby delivering to the cell the DNA capable of being expressed therein.

The examiner relies upon the following references:

Powell et al. (Powell)	5,877,159	Mar. 02, 1999

Claims 45-55 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent 5,824,538. In addition, claims 45-55 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Powell. After careful review of the record and consideration of the issues before us, we affirm the obviousness double patenting rejection. We vacate, however, the rejection of the claims under 35 U.S.C. § 102(e). We do agree with the examiner that the Powell reference is applicable to the subject matter of claims 45-51, 53 and 54, and thus new

grounds of rejection are herein set forth under 37 CFR. § 1.196(b) as to those claims.

BACKGROUND

The claimed invention is drawn to a method of introducing exogenous DNA into an animal cell using a bacterial delivery system. Upon entry into the cell, the bacteria will undergo lysis, thereby delivering the exogenous DNA to the animal cell.

According to the specification:

> These unique bacterial delivery systems therefor [sic] can be used as vaccines to prevent or treat infectious diseases and cancer, down regulate the immune system in the case of tissue rejection in transplantation, prevent or treat autoimmune disease and other diseases related to dysregulation of the immune system. In addition, the bacterial delivery systems can be used for gene therapy or gene replacement for treatment or amelioration of disease such as hereditary genetic diseases, cancers and virus infections.

Id. at 1.

In a preferred embodiment, the bacteria is an attenuated Shigella strain, that again, undergoes lysis upon entry into the animal cell. See id. at 4. The specification teaches that:

> A mutation in the gene encoding aspartate β-semialdehyde dehydrogenase (ASD) was placed in Shigella flexneri 2a strain 2457T for the specific purpose of delivering DNA to mucosal epithelial cells of the gut. This resulted in a strain unable to grow in the absence of diaminopimelate (DAP), an essential peptidoglycan component comprising the cell wall of gram negative bacteria. DAP is not present in mammalian tissues, and is therefore unavailable for scavenge by infecting bacteria. This mutant strain of Shigella represents a highly attenuated bacterial vector, which is capable of invading mammalian cells and providing protective immunity against strain specific Shigella infection, as well as

> serving as a delivery vehicle for oral and other mucosal DNA immunization and gene therapy strategies.

Id. at 5.

DISCUSSION

Obviousness-Type Double Patenting

Claims 45-55 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent 5,824,538. See Examiner's Answer, page 2. Appellants have indicated their willingness to file a terminal disclaimer at the time the claims have otherwise been deemed to be allowable. See Appeal Brief, page 3. Because appellants have not argued the merits of the rejection, and because a terminal disclaimer has not been filed, the rejection is affirmed.

35 U.S.C. § 102(e)

Claims 45-55 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Powell. According to the rejection:

> Powell [ ] broadly disclose[s] and claim[s] delivery of live, invasive bacteria which are attenuated by a variety of means and which also comprise a "eukaryotic expression casette encoding genes." The purpose of the "eukaryotic expression cassette" that the animal cell infected by the invasive bacteria will express the cassette and produce an antigen which acts as a vaccine. At column 6, starting at line 48, Powell [ ] teach[es] that the present invention provides the first documentation of genetic exchange between live, invasive bacteria, and animal cells. That is, once the bacteria deliver the eukaryotic expression cassette, it is the animal cells which express and produce the gene products (see line 57-2). Clearly, in order for the animal cell to express the eukaryotic expression cassette, the cassette must be released by the bacteria inside the animal cell—which is what happens upon lysis of the

> bacterial cell. It is further noted that because the bacteria cannot express the eukaryotic expression cassette, the expression observed by Powell [ ] comes from the expression of the cassette by the animal cell.
>
> This is the same concept used by Appellant in the instant application for the "delivery of exogenous DNA capable of being expressed in an animal cell." At columns 7 and 8 of the patent, Powell [ ] teach[es] that bacteria are used to deliver eukaryotic expression cassettes to animal cells or animal tissue and that the cassette is introduced and expressed in animal cells. At column 24, example 4, Powell [ ] teach[es] that the Δasd attenuating mutation of bacteria (S. flexneri) which results in lysis of bacterial cells in the absence of DAP (D,L-α, ε-doaminopimelic acid). Since DAP is not found in eukaryotic animal cells, bacteria which are delivered to animal cells and/or tissues will lyse.

Examiner's Answer, pages 3-4.

We agree with the examiner that Powell is relevant to the patentability of the claims. The Panel notes, however, that the examiner has employed a "shot-gun" rejection, where a claim-by-claim analysis should have been employed. The deficiencies of the examiner's rejection are summed up by the statement that Powell teaches "the same concept used by Appellant in the instant application for the 'delivery of exogenous DNA capable of being expressed in an animal cell.'" A rejection should be addressed to the claimed invention, and not the "concept" disclosed by the application. Moreover, given the fact situation in the instant application, i.e., that the examiner is asserting that Powell is "broadly" claiming the instant invention, and thus priority of invention can only be established through interference proceedings, the rejection also needed to specifically address the subject matter claimed by Powell and explain how the

instant claims are drawn to the same patentable invention. We therefore vacate the examiner's rejection and set forth the following new grounds of rejection under 37 CFR § 1.196(b).

Rejection under 37 CFR § 1.196(b) of Claims 45-51, 53 and 54

Claims 45-51, 53 and 54 are rejected under 35 U.S.C. § 102(e) as described by Powell.

Claim 45 is drawn to a method for the delivery of exogenous DNA that is capable of being expressed in an animal cell. The method comprises the steps of: 1) introducing the DNA into a mutated bacteria, wherein the bacteria has a attenuating factor that results in lysis of the bacteria after entry into the animal cell; and 2) administering the bacteria to the cell, such that the bacteria, once inside the cell, will lyse, thus delivering the exogenous DNA to the cell.

Claims 1, 5 and 6 of Powell recite:

> 1. A method for introducing and expressing a gene in animal cells comprising infecting said animal cells with live invasive bacteria, wherein said bacteria contain a eukaryotic expression cassette encoding said gene, wherein said gene encodes a vaccine antigen wherein said vaccine antigen is expressed at detectable levels, and wherein said animals cells are cultured in vitro.
>
> 5. The method of claim 1, wherein said invasive bacteria is selected from the group consisting of Shigella spp, Listeria spp., Rickettsia spp and enterovasive Escherichia coli.
>
> 6. The method of claim 5, wherein said invasive bacteria is attenuated.

Claim 1 of Powell differs from instant claim 45 by not specifically reciting that the DNA to be expressed in the animal cells is introduced into the bacteria; by specifying that the expressed DNA is a vaccine antigen; and by not specifying that the attenuating factor results in lysis of the cell.

In order to construe the claims and determine what is encompassed by the claim language, we must look to the specification. See Ethicon Endo-Surgery, Inc. v. US Surgical Corp., 93 F.3d 1572, 1578, 40 USPQ2d 1019, 1023 (Fed. Cir. 1996) (noting that one may look to the specification to aid in the interpretation of a term already in the claim).

Although claim 1 of Powell does not specifically recite that the DNA to be expressed in the animal cells is introduced into the bacteria, the Powell specification teaches introducing a eukaryotic expression cassette into a mutated bacteria. See column 24, lines 6-11. Moreover, eukaryotic expression cassette are not a normal part of the bacterial genome, therefore introducing the eukaryotic expression cassette is implicit to the method of claim 1 of Powell.

Claim 45 of the instant application does not limit the exogenous DNA to a specific function, such as a vaccine antigen as required by claim 1 of Powell. The instant specification, however, teaches that the bacterial delivery system may be used "as vaccines to prevent or treat infectious diseases and cancer," thus one of ordinary skill would read "exogenous DNA" as used by instant claim 45 as encompassing vaccine antigens as specified in claim 1 of Powell.

Finally, although Powell does not specifically claim that the bacteria contains an attenuating factor that results in lysis of the bacteria, claim 6 specifies that the invasive bacteria is attenuated. Example 4 of Powell, at column 24, teaches bactofection experiments using an attenuated bacteria—a S. flexnari strain of bacteria having a Δasd attenuation. See Column 24, lines 5-46. The Δasd attenuation results in the lysis of the bacteria in the absence of DL-α,ε-diaminopimelic acid (DAP), and DAP is not present in eukaryotic cells. Thus, one of ordinary skill in the art would understand that "attenuated" as recited in claim 6 of Powell includes an attenuation that results in lysis of the bacteria upon introduction into an animal cell.

Thus, claim 6 of Powell and claim 45 of the instant application are drawn to the same patentable invention. The Sizemore declaration, submitted under 37 CFR § 1.131, see Paper No. 20, is thus not sufficient to remove the Powell patent as a reference, as section 131(a) specifies that:

> Prior invention may not be established under this section if . . .
>
> (1) The rejection is based upon a U.S. patent or U.S. Patent application of a pending or patented application to another or others which claims the same patentable invention as defined in § 1.601(n).

Claim 46 of the instant application is also drawn to the same patentable invention of Powell, as Example 4, as described above, is drawn to bactofection of mammalian cells, such as HeLa cells. Claims 47, 48 and 49 of the instant application are also not patentably distinct as one of the strains used in the

examples of Powell, see e.g., Example 4, is S. Flexneri, thus one of ordinary skill in the art would understand that S. Flexneri strains, such as 15D,[1] are encompassed by the claimed invention of Powell.

Claim 50 of the instant application is also drawn to the same patentable invention as Powell, as claim 15 of Powell is drawn to a method similar to claim 1 of that patent, wherein the invasive bacteria is administered to a mucosal surface of the animal. As the Powell specification teaches that an example of a mucosal surface is the intestine, one of ordinary skill would read "mucosal surface" as used in claim 15 of Powell as encompassing an intestinal mucosal surface. Therefore, claim 51 of the instant application is drawn to the same patentable invention as Powell.

Finally, claims 53 and 54 are drawn to the same patentable invention as claimed by Powell. The Δasd attenuation as disclosed in example 4 of Powell, see the discussion supra with respect to instant claim 45, is drawn a mutation of the active aspartate β-semialdehyde dehydrogenase of the DAP pathway. See, e.g., page 9 of the instant specification, discussing the asd mutation. As noted in the previous paragraph, claim 15 of Powell teaches delivery of the attenuated bacteria to a mucosal surface, such as an intestinal mucosal surface, as required by the instant claims.

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[1] Moreover, we note that appellants do not argue that the use of the 15D strain renders instant claim 49 patentably distinct over the claims of Powell.

As Powell does not claim that the Shigella is further inactivated, claims 52 and 55 are free of the rejection over Powell.

In addition to affirming the examiner's rejection of one or more claims, this decision contains a new ground of rejection pursuant to 37 CFR § 1.196(b), by final rule notice, 62 Fed. Reg. 53,131, 53,197 (Oct. 10, 1997), 1203 Off. Gaz. Pat. & Trademark Office 63, 122 (Oct. 21, 1997)). 37 CFR § 1.196(b) provides, "A new ground of rejection shall not be considered final for purposes of judicial review."

> Regarding any affirmed rejection, 37 CFR § 1.197(b) provides:
>
> (b) Appellant may file a single request for rehearing within two months from the date of the original decision . . . .

37 CFR § 1.196(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of proceedings (37 CFR § 1.197(c)) as to the rejected claims:

> (1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner. . . .
>
> (2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record. . . .

Should the appellant elect to prosecute further before the Primary Examiner pursuant to 37 CFR § 1.196(b)(1), in order to preserve the right to seek review under 35 U.S.C. §§ 141 or 145 with respect to the affirmed rejection, the effective date of the affirmance is deferred until conclusion of the prosecution before the examiner unless, as a mere incident to the limited prosecution, the affirmed rejection is overcome.

If the appellant elects prosecution before the examiner and this does not result in allowance of the application, abandonment or a second appeal, this case should be returned to the Board of Patent Appeals and Interferences for final action on the affirmed rejection, including any timely request for rehearing thereof.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED; 37 C.F.R. § 1.196(b)

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